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The Value of Antistreptococcic  
Serum in the Treatment of  
Puerperal Infection

(REPORT OF THE COMMITTEE OF THE AMERICAN GYNECOLOGICAL SOCIETY, MAY, 1898)

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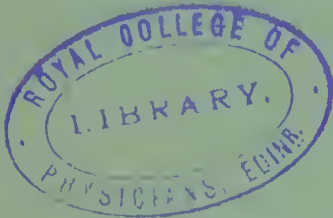
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## THE VALUE OF ANTISTREPTOCOCCIC SERUM IN THE TREATMENT OF PUERPERAL INFECTION.

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### I.

YOUR Committee have to report that during the past year they have considered the question of the efficacy of antistreptococcic serum in the treatment of those forms of puerperal fever due to streptococcus infection. They regret, however, that the experimental work which they have begun upon the subject is not yet concluded, and that they are, therefore, compelled to base their present report upon a careful study of the literature upon the subject, and their personal experience in the treatment of streptococcic puerperal infection, reserving for a later report the results of their experimental work.

In the present report, your Committee will give in the first place a brief review of the history of antistreptococcic serum, and will then consider the results obtained by the various observers who have used it in the treatment of puerperal infection. We shall then consider the experimental work which has been done upon the subject and its bearing upon the results obtained at the bedside. And, after having reviewed the literature upon the subject, we shall consider the personal experience of members of your Committee in the treatment of streptococcus infection during the puerperium; and, finally, we shall combine the results of our own work with our literary studies, and attempt, if possible, to deduce therefrom certain conclusions for our guidance in the treatment of such cases in the future.

Although many investigators had previously studied the question of immunity, and attempted to cure streptococcic infection by the use of serums, the history of antistreptococcic serum practically began on February 23, 1895. For, on that date, Marmorek presented a communication to the Société de Biologie of Paris, in which he stated that he had been able so to increase the virulence of streptococci that they would always produce death in rabbits, and that he was at that time engaged in the preparation of an efficient antistreptococcic serum.

He showed that streptococci ordinarily lose their original virulence with great rapidity in ordinary bouillon cultures, but that they would retain it when cultivated in a mixture of two parts of bouillon and one of human blood serum; and stated that by the use of this culture medium, in connection with the usual methods of increasing the virulence of streptococci, by passing them repeatedly through the bodies of animals, he had been able to raise their virulence to such an extent that the one hundred billionth part of a cubic centimetre of a bouillon and blood serum culture would kill a rabbit within twenty-four hours.

When experimenting with such infinitesimal doses of this very virulent organism, he found that only one rabbit out of four died, but that they all died when the one hundred millionth of a cubic centimetre was administered; and he attributed this apparent contradiction to the fact that in the first-mentioned dose he had reached the physical limit of dilution. So that in all probability many doses were so dilute as not to contain a single streptococcus. But death was certain when a single one of the very virulent streptococci was present.

At the same meeting, Charrin and Roger announced that they had succeeded in producing an efficient antistreptococcic serum by injecting into mules large quantities of sterilized cultures of streptococci; and stated that on February 6 they had successfully treated a case of puerperal fever with it, and in a footnote mentioned that they had obtained very good results from its use in another case.

A few weeks later, Marmorek presented a second communication upon the subject, in which he stated that he used his serum in 46 cases of erysipelas with most beneficial results.

In the July number of the *Annales de l'Institut Pasteur* for 1895, he published a long article in which he gave a detailed account of the methods which he employed in preparing his serum, and reported the results which he had obtained by its

use in the treatment of 413 cases of erysipelas in Chantemesse's clinic, in which the mortality was only 3.4 per cent.

He also stated that he had treated 16 cases of puerperal fever by the same method. In all of these cases, he examined the uterine discharges bacteriologically and refrained from local treatment while using the serum. In 7 cases he had to deal with a pure streptococcic infection, and all of them recovered. In 3 other cases the streptococcus was combined with the colon bacillus, and all of them died. In 5 other cases the staphylococcus was associated with the streptococcus, and of these 2 died. While in the last case, in which the infectious agent was the colon bacillus, the serum appeared to have no effect.

From his experience in 16 cases, he concluded that his serum was a most efficacious means of treatment in cases of pure streptococcus puerperal infection, but that it was useless if other organisms were combined with it; as in such cases the serum could only neutralize the effects of the streptococcus, but could not be expected to have any effect upon the organisms associated with it.

He therefore concluded that the first essential in the treatment of puerperal infection was the bacteriological examination of the uterine secretions, as one could only expect the serum to be beneficial in the cases which were positively due to the streptococcus; and that successful results could only be anticipated when the use of the serum was begun at a sufficiently early period, it being understood that all local treatment, such as douches and curettage, should be abandoned during its employment.

Marmorek's article excited the greatest possible interest, and the hope was universally expressed that subsequent experience would demonstrate the correctness of his claims. In a short time many observers made use of the serum in the treatment of puerperal infection, not to mention its use in various other forms of streptococcic infection, such as erysipelas, scarlet fever, angina, etc.

In April, 1896, Charpentier was able to report to the Obstetrical Society of France 40 cases of puerperal infection, not including Marmorek's 16 cases, in which antistreptococcic serum had been employed by the following observers: Roger and Charrin, Gaulard, Merigot de Treigny, Ribemont-Desaignes, Martellière and Charpentier, Maygrier, Bar, Porak, Budin, and Vinay. Of the 40 cases, only 24 recovered. Five of the fatal cases were of no value in considering the effects



of the serum, as they were moribund when first seen, thus leaving 35 available cases with 12 deaths, a mortality of 35.29 per cent. Not all of these cases were examined bacteriologically, and, on analyzing those which were, he found that streptococci were demonstrated in pure culture in 16 cases, of which 7 died; while in 8 other cases the streptococcus was associated with either the staphylococcus or colon, or both, of which 4 died; thus making a total mortality of 11 out of 24 cases, or nearly 48 per cent.

After such a showing, Charpentier was naturally not very enthusiastic, especially as Gaulard believed that the use of the serum had hastened the death of one of his patients, and as the experience of the other observers had shown that its use was not unattended by danger; for several of them had observed local abscesses and an increase in the amount of albumin in the urine after its use, not to speak of a very troublesome erythema in some cases. Charpentier, therefore, concluded that the results following its employment were not as brilliant as he had been led to expect, and, while it might be used in appropriate cases, he believed that Marmorek's advice to discard all local treatment during its employment could not be conscientiously followed.

In the discussion which followed this paper, most of the speakers indorsed Charpentier's conclusions, and Budin went so far as to state that he considered the serum absolutely useless. At the same meeting, Charpentier's statements were abundantly confirmed by Bar and Tissier, who three months later published in *L'Obstétrique* a long article upon the subject, in which they stated that the results obtained by its use were far from satisfactory.

The unfavorable opinion elicited in this discussion did not, however, prevent large numbers of observers from continuing the use of the serum, especially in France and Great Britain, while it was comparatively little used in this country and hardly at all in Germany.

Its very limited use in Germany was probably due to the influence of Petruschky, who stated, as the result of his experiments in the Hygienic Institute of Berlin, that Marmorek's serum, as well as one prepared in Lyons, was absolutely inefficient, and that their use upon human beings could not be recommended. Similar views were also expressed by Lubarsch.

Indeed, the only German who has reported the use of anti-

streptococcic serum in any number of cases is Savor, who employed it in 15 cases of puerperal infection which occurred in Chrobak's clinic in Vienna, with 1 death. In spite of these apparently favorable results, however, he concluded that it had very little influence upon the course of the infection, but at the same time stated that he had observed no ill effects from its use and would continue to experiment with it in appropriate cases.

We have collected from the literature, as far as possible, all cases of puerperal infection in which antistreptococcic serum has been used up to the first of April, 1899, and we find that it has been used in France by twenty-seven observers in 214 cases, in Germany by one observer in 15 cases, and in Great Britain and this country by many observers in 123 cases, making a total of 352 cases treated up to the present time.

TABLE OF CASES TREATED WITH ANTISTREPTOCOCCIC SERUM.

*Cases in which a Bacteriological Diagnosis was made.*

## CONTINENTAL.

Observer.	No. of cases.	Cures.	Deaths.	Observer.	No. of cases.	Cures.	Deaths.
Ausset and Rouzé.....	1	1	0	Laruelle .....	1	1	0
Bar and Tissier.....	13	5	8	Marmorek .....	15	10	5
Budin .....	4	2	2	Martellière and Char-			
Bué .....	1	1	0	pentier .....	1	1	0
Butin .....	2	2	0	Paté (Bar) .....	8	4	4
Dubrisay.....	1	1	0	Queirel .....	1	1	0
Durante and Siron....	1	1	0	Savor .....	15	14	1
Flandrin .....	1	1	0	Wallich .....	2	0	2
Gaulard .....	1	0	1	Weinstein .....	1	0	1
Laran (Ribemont-Des-							
saignes).....	1	1	0				

## ENGLISH AND AMERICAN.

Brack .....	1	1	0	Norris .....	1	1	0
Dobbin. ...	1	1	0	Paddock .....	1	1	0
Douglas .....	1	0	1	Raw .....	3	1	2
Edmunds.....	1	1	0	Raw ..	1	1	0
Fry .....	3	1	2	Reddy .....	1	1	0
Groth .....	1	1	0	Saunders.....	4	3	1
Hastings .....	1	1	0	Sharp.....	1	1	0
Haultain .....	2	1	1	Shaw .....	1	1	0
Lockhart .....	1	1	0	Shoemaker .....	1	0	1
Marx .....	1	0	1	Steele .....	2	2	0
Mumford .....	1	1	0	Williams, J. D.....	1	1	0

Total, 101 cases, 33 deaths, a mortality of 32.69 per cent.

*Cases in which a Bacteriological Diagnosis was not made.*

## CONTINENTAL.

Observer.	No. of Cases.	Cures.	Deaths.	Observer.	No. of Cases.	Cures.	Deaths.
Bar and Tissier.....	2	0	2	Ledrain .....	1	1	0
Berthod .....	1	1	0	Lop .....	2	2	0
Charrin and Roger....	2	2	0	Maygrier.....	2	0	2
Gaulard .....	1	1	0	Merigot de Treigny....	1	1	0
Jacquart .....	1	1	0	Porak .....	3	2	1
Josué and Hermany...	1	1	0	Queirel .....	14	12	2
Laran (Ribemont-Des-saignes) .....	23	18	5	Wallich .....	102	99	3
				Vinay .....	3	2	1

## AMERICAN AND ENGLISH.

Andrew .....	1	1	0	Lockhart.....	1	0	1
Adam .....	1	1	0	Mapleton.....	1	1	0
Baldy. . . . .	1	0	1	McKerron.....	3	2	1
Campbell.....	1	1	0	McNalty .....	1	1	0
Campbell.....	1	1	0	Montgomery .....	3	3	0
Clark .....	1	1	0	Montgomery .....	1	1	0
Coombs .....	1	0	1	Moorhead. . . . .	1	1	0
Cummins.....	1	1	0	O'Conner .....	1	1	0
Cuscaden .....	1	1	0	Paddock .....	1	1	0
" T. C." .....	1	0	1	Pim.....	2	2	0
Davis .....	3	1	2	Raw .....	1	0	1
Durno .....	1	1	0	Rawlins .....	1	0	1
Eakins.....	1	1	0	Richmond .....	2	2	0
Edgar .....	1	1	0	Roughton.....	1	0	1
Fowler.....	1	1	0	Russell.....	1	1	0
Frazer .....	1	1	0	Sheen .....	1	0	1
Fry (table).....	17	10	7	Siff .....	1	1	0
Gregg .....	1	1	0	Smith .....	1	1	0
Hayward.....	1	1	0	Stansby .....	2	2	0
Henry.....	1	0	1	Steele .....	1	0	1
Henry.....	1	1	0	Thomas.....	4	3	1
Hill .....	1	1	0	Thomas .....	1	1	0
Howard .....	1	1	0	Veitch .....	1	1	0
Hirst .....	3	2	1	Walsh .....	1	1	0
Johnston .....	2	2	0	Whittingdale.....	1	1	0
Jackson .....	1	1	0	Williams, C. E.....	1	1	0
Kennedy . . . . .	1	1	0	Williams, J. D.....	5	4	1
Kershaw .....	1	1	0	Work .....	1	0	1
Leask.....	1	1	0				

Total, 251 cases, 40 deaths, a mortality of 15.85 per cent.

*Summary.*

101 cases with bacteriological examination, with 33 deaths, 32.69 per cent.

251 " without " " " 40 " 15.85 "

Total, 352 cases with 73 deaths, a mortality of 20.74 per cent.

On inquiring as to the results obtained, we find that 279 cases recovered and 73 cases died, a mortality of 20.74 per cent,



which we must admit is not sufficiently low to encourage us to proceed further with its use. It may be urged, perhaps, that we are not justified in drawing conclusions from such statistics, as in many cases bacteriological examinations were not made, and in some instances, at least, the cases were moribund when the serum was administered.

On analyzing the cases thus far reported, we find that eighteen French and German observers treated 70 cases, in which a bacteriological examination had been made and streptococci found, with 24 deaths, or a mortality of 34.28 per cent; and twenty-one English and American observers treated 31 similar cases with 9 deaths, a mortality of 29 per cent, making a total of 101 cases with 32.69 per cent mortality.

We also find that fifteen French observers treated 159 cases without bacteriological examination with 16 deaths, a mortality of 16.65 per cent; while fifty-four American and English observers treated 92 similar cases with 24 deaths, a mortality of 26 per cent, thus making a total of 251 cases, which were not examined bacteriologically, with 15.85 per cent mortality.

It is apparent that the better results in the latter group of cases are due to the fact that in it were included many cases which were not due to streptococcus infection, which in all probability would have recovered without treatment; as it is well known that only a certain proportion of rises of temperature in the puerperium are due to streptococcus infection, Williams having found only 23 streptococcus cases in 91 rises of temperature in the puerperium, 25 per cent. and Krönig 56 in 296 cases, 19 per cent.

We shall probably overestimate the frequency of streptococcus infection in the 251 cases which were not examined bacteriologically, if we calculate that one-third of them were of that nature, which would give 84 such cases. Admitting that practically all the deaths in this series occurred in streptococcus cases, we find 84 such cases, with 40 deaths, or 48 per cent, which is a considerably higher mortality than in the cases in which streptococci were positively demonstrated.

In considering these figures, however, we must remember that many of the reports are based upon one or two severe cases, which the observers treated with serum, while their milder cases recovered without its employment. Such reports would naturally give an exaggerated idea of the mortality and will not be considered.

Accordingly, we shall deal only with the results of those

observers who based their reports upon a considerable number of cases, and we find that seven observers—*i.e.*, Savor, Bar and Tissier, Paté, Queirel, Marmorek, Wallich, and Laran—treated 196 cases, 55 of which were examined bacteriologically, while 141 were not. Of the former 36.36 per cent died, and of the latter only 8.5 per cent. It is accordingly apparent that the results of these observers in the treatment of pure streptococcus cases are not better, but, if anything, rather worse, than those shown by our general statistics.

Another method of obtaining an idea as to the curative value of the serum is to ascertain the opinions of the various authors who have employed it. This we have done with the French and German observers, and we find that fourteen out of the twenty-eight express a favorable and the rest an unfavorable opinion concerning it.

*Favorable Opinions.*

Ausset and Rouzé.  
Berthod.  
Bué.  
Butin.  
Charrin and Roger.  
Jacquart.  
Josué and Hermany.  
Ledrain.  
Laran.  
Laruelle.  
Lop.  
Marmorek.  
Queirel.  
Weinstein.

*Unfavorable Opinions.*

Bar and Tissier.  
Budin.  
Dubrisay.  
Durante and Siron.  
Flandrin.  
Gaulard.  
Martelliére and Charpentier.  
Maygrier.  
Merigot de Treigny.  
Paté.  
Porak.  
Savor.  
Vinay.  
Wallich.

It would accordingly appear that definite conclusions cannot be reached in this manner. But, on considering the reports more closely, we find that this supposition is not correct; for we find that eleven of the fourteen authors, who expressed a favorable opinion, treated only 13 cases altogether; while the other three, Marmorek, Laran, and Queirel, treated 54 cases with 12 deaths, a mortality of 22 per cent. We find, however, that neither Laran nor Queirel examined their cases bacteriologically, and it is more than likely that a large proportion of their cases were not due to streptococcus infection, but to other causes. So that Marmorek is the only author among them whose statistics are of value, and we have already shown that his results leave a great deal to be desired.

The other fourteen observers, on the contrary, state that the serum was useless, and in rare cases even harmful to their patients. Thus, we find that Gaulard attributed the death of one of his patients to the use of the serum, and stated that, while her temperature fell after its administration, she went into a condition of collapse from which she did not rally.

Similar statements were also made by Bar and Tissier, and Charpentier, both of whom also stated that the deleterious effects of the serum may be manifested by painful swellings at the seat of the inoculation, by marked rises of temperature immediately following its use, and that it may lead to abscess formation and give rise to erythema and urticaria a varying length of time after the injection, and in rare instances may cause the death of the patient from collapse.

A number of authors, among whom may be mentioned Dubrisay, Laran, Paté, and Van de Velde, state that abscesses developed at the seat of injection in a number of their cases. Several explanations have been advanced to explain their production. Van de Velde considers that they are usually due to the presence of streptococci in the serum, which he was able to demonstrate in two out of four samples of Marmorek's serum which he examined. Laran, on the other hand, does not believe that the abscesses are due to the use of a contaminated serum, but rather to a chemotactic influence which it exerts, by which streptococci which are circulating in the blood are attracted to the seat of inoculation. We are not prepared to state which of these explanations is correct; but the fact remains that abscesses very frequently follow its use.

All the authors who have written upon the subject do not agree concerning the deleterious effects of the serum, and we find Savor, Wallich, Weinstein, and others stating that they have employed it in a large number of cases without observing the slightest ill effects from its use. Its innocuousness is particularly demonstrated by the experience of Wallich, who employed it in about 400 cases without observing any untoward symptoms.

In spite of the fact that Wallich has shown that the serum is harmless as far as the patient is concerned, his observations in the Baudelocque clinic in Paris show that it is very inefficient both in the prophylactic and curative treatment of puerperal infection. During the year 1896, he tested the serum upon a large number of cases, and administered it to every patient entering the hospital in whom there was the slightest possibility



of infection. He administered serum to 383 women suspected of infection on entrance, but nevertheless 58 of them developed well-marked infectious symptoms. The total number of cases of infection which occurred in the hospital during the year was 179, and the cases which were treated prophylactically constituted 32 per cent of that number.

He also employed the serum, in conjunction with the usual methods of treatment, in the cases which were definitely infected, and found that the results were no better than in the years in which it was not used, as the mortality from sepsis during the years 1895, 1896, and 1897 was 0.18, 0.24, and 0.22 per cent respectively, the serum having been used only in the latter year.

It is apparent from the figures and the statements which we have just adduced that the clinical results obtained by the employment of antistreptococcic serum in the treatment of puerperal sepsis leave a great deal to be desired, and are apparently no better than before its introduction.

Turning from the purely clinical side, we find that a large amount of experimental work has been done upon the subject and that Marmorek's original work has been repeated and tested by numerous investigators with varying results.

Petruschky, working in the Hygienic Laboratory in Berlin with streptococci and serum which were furnished him by Marmorek, arrived at absolutely contradictory conclusions; and, as a result of his experiments, stated that Marmorek's serum had shown itself absolutely inefficient in the laboratory and that its use at the bedside could not be recommended.

Aronsohn, on the other hand, likewise working in Berlin, conceived a more favorable opinion of Marmorek's work, and was inclined to believe that Petruschky's results were due to the fact that he had employed a serum which had become inert through age. For he stated that he had succeeded in raising the virulence of streptococci to a very marked degree and had prepared from them a very efficient antistreptococcic serum. After putting this aside for a few months, and again experimenting with it, he was surprised to find that it was absolutely inert. But upon preparing a fresh serum from the same streptococcus, he found that it was decidedly efficacious.

Bullock, working in England, found that he could readily raise the virulence of streptococci and prepare an efficient serum, but demonstrated at the same time that a serum



prepared from a given streptococcus was not necessarily effective against a streptococcus obtained from a different source.

The streptococcus, as is well known, is an extremely variable organism, and we can all remember the early attempts to make a distinction between the streptococcus pyogenes and the streptococcus of erysipelas. It was gradually demonstrated, however, that these two varieties of streptococcus are essentially the same, and we no longer attempt to distinguish between them.

At the same time, however, there are very marked differences between individual streptococci, which are manifested by their varying virulence, their morphology, their behavior on culture media and toward the various coloring matters. Thus, one streptococcus may be absolutely inert, while another is intensely virulent. One streptococcus may grow upon potato, while the majority do not. And in very rare instances they may decolorize by Gram's method of staining (Etienne, Doléris and Bourges, Nocard and Mollereau). The difference in morphology is occasionally very marked, so that certain authors have attempted to differentiate the streptococcus longus from the streptococcus brevis, etc.

The general consensus of opinion, however, is that while streptococci may present very marked differences among themselves, they still belong to the same group of organisms, and that we are not justified at present in attempting to divide them into various groups; as it is well known that we can often change the biological properties of individual streptococci and can markedly alter their virulence by appropriate procedures. We accordingly find that Lemoine, Marmorek, Widai and Bezançon, Etienne, and others in France have adopted this view, and Lubarsch in his recent article upon the subject expresses a similar opinion.

While we believe in a general sort of way that all forms of streptococci belong to the same general family, the great bulk of the experimental work upon antistreptococcic serum appears to show that there are marked differences in the behavior of various streptococcus infections when treated with antistreptococcic serum. Thus, for example, Méry and Lorraine, Courmont, Desse, Van de Velde, and others have shown that a serum which is produced from a certain streptococcus may be extremely efficacious against infections due to that particular organism, but absolutely inert against infections produced

by streptococci which have been obtained from other sources. Indeed, Desse and Courmont have shown that in rare instances a serum obtained from a certain streptococcus may predispose an animal to infection with another streptococcus instead of rendering it immune.

Van de Velde goes so far as to state that a serum obtained from an individual streptococcus is of little or no value in the treatment of streptococcus infections, as we possess no means of ascertaining in advance whether the streptococcus in question will be affected by the serum or not. And to overcome this difficulty, he suggests that the serum be prepared, not from a single streptococcus, but from a number of streptococci obtained from different sources; so that its efficiency will not be limited to infections due to a particular variety of streptococcus, but that it may offer some chance of being effective no matter what may be the character of the streptococcus which has given rise to the infection. He has prepared such a serum, and designated it as a serum polyvalent, and recommends its use at the bedside. It appears to us, however, that this is begging the question, and, if his statements are borne out, that the entire doctrine of antistreptococcic serum rests upon so insecure a foundation and is associated with such elements of chance that its employment in clinical work cannot be advocated.

Marmorek, on the other hand, is a marked believer in the unity of streptococci, and believes that a serum which is prepared from one virulent streptococcus will be efficient against all other varieties of that organism. And in this statement he is borne out by the experiments of Bullock, Lemoine, and others.

It is apparent, however, that the doctrine of antistreptococcic serum has received a marked blow from the work of Courmont, Desse, and Van de Velde, and this, taken in connection with the comparatively poor results which have been obtained by its employment in clinical work, does not appear to justify us in recommending its use at the bedside, as it would appear to be necessary to identify the streptococci in any given case and to be provided with an appropriate serum for their treatment.

As far as your Committee can see, the only undisputed point which has thus far been elicited by the work which has been done upon antistreptococcic serum is that Marmorek has provided us with a method by which we can raise the virulence of certain streptococci to an almost inconceivable extent.

After a careful study of the literature, it appears that we are justified in formulating the following conclusions concerning the present status of antistreptococcic serum:

1. Clinical observation has shown that the results obtained by its employment leave a great deal to be desired and apparently indicate that it has little, if any, effect upon the general course of streptococcic puerperal infection.

2. The results of laboratory work have been extremely conflicting and have cast grave doubts upon the entire subject. The serum polyvalent of Van de Velde cannot be considered as a satisfactory solution of the difficulty, as it is impossible to foretell in a given case whether any of the serums composing it will be efficient against the particular streptococcus with which one has to deal.

3. The only positive fact which has thus far been satisfactorily demonstrated is the possibility of markedly increasing the virulence of streptococci by appropriate methods.

Passing from the study of the literature upon the subject to the experience of the members of your Committee in the treatment of undoubted cases of streptococcic puerperal infection, we find that Dr. Williams has treated 23 such cases, Dr. Pryor 14, and Dr. Fry 8 cases. Each of these gentlemen, however, has treated his cases by different methods, Dr. Fry being the only one who has employed antistreptococcic serum. All of the cases were undoubtedly streptococcic in origin, as was demonstrated by the bacteriological examination of the uterine lochia, which were obtained by means of Döderlein's tube.

In this report, we shall give the results of Dr. Williams' work somewhat in detail, and refer for particulars concerning the work of Dr. Pryor and Dr. Fry to their supplementary articles, which are appended to this report.

During the past three years Dr. Williams has examined bacteriologically the uterine lochia of 91 puerperal cases, the examination being made when the temperature reached  $101^{\circ}$  in the hospital cases and  $102^{\circ}$  in the out-patient and consultation cases. In this number of cases, streptococci were demonstrated 23 times, 25 per cent. In 16 cases streptococci were present in pure culture; in 2 cases an anaerobic variety of streptococcus was cultivated, and in 5 other cases the streptococcus was associated with other organisms. In these 5 cases the bacteriological findings were as follows:

- (1) Streptococcus, colon bacillus, and an unidentified anaerobic bacillus.



(2) *Streptococcus*, *staphylococcus aureus*, *bacillus typhosus*, and *bacillus aerogenes capsulatus*.

(3) *Streptococcus*, *staphylococcus aureus*, colon bacillus, and *bacillus aerogenes capsulatus*.

(4) *Streptococcus* and colon bacillus.

(5) *Streptococcus*, *staphylococcus aureus*, and an unidentified gas-producing bacillus.

Of the entire 23 cases, the last is the only one which died.

Some idea of the severity of the cases may be obtained from the following table, which shows the highest temperature which was reached in each case: In 4 cases the temperature ranged between 102° and 102.9°; in 6 cases between 103° and 103.9°; in 8 cases between 104° and 104.9°; in 1 case between 105° and 105.9°; in no cases between 106° and 106.9°; and in 2 cases the temperature reached 107°.

None of the cases had peritonitis. All of them presented a more or less marked endometritis, and in 3 cases marked pyemia was present, which was accompanied by abscess formation in various portions of the body, from the pus of which streptococci were cultivated in each instance.

Classifying the cases according to the impression which they made upon us at the bedside, we would say that 10 cases were very sick and caused us considerable apprehension; 6 cases were moderately and 7 cases were only slightly sick.

The treatment which was pursued in these cases was as follows: As soon as the temperature reached 101° F. in the hospital cases, or 102° F. in the outside cases, the uterine lochia were removed by Döderlein's tube under the strictest aseptic precautions. The sterile finger was then introduced into the uterine cavity and its walls carefully palpated. If they were markedly roughened, a probable diagnosis was made of infection with putrefactive organisms, either alone or in combination; while if its walls were smooth to the examining finger, the existence of a streptococcus infection was rendered quite probable. In none of the cases under consideration was enough necrotic material found in the uterine cavity to justify curettage. After examining its interior with the finger, the uterus was douched with four or five litres of sterile salt solution.

The tube containing a sample of the lochia was then taken to the laboratory, where cultures were made. If the presence of streptococci was demonstrated, no further local treatment was employed and the patient left to herself as much as possible.



If her general condition was good, no medicinal treatment was employed. But if the patient showed signs of exhaustion, she was immediately treated with large doses of strychnia and alcohol, together with as vigorous a diet as she could well stand. Indeed, we may say that strychnia and alcohol were used in such doses as to keep the patient almost on the verge of strychnia poisoning and drunkenness.

The result of this method of treatment, as we have already indicated, was one death out of 23 cases, a mortality of 4.35 per cent. In 6 cases the temperature fell immediately after the douching and did not rise again; while in the remainder of the cases it persisted for a varying length of time, and in several of the pyemic cases it lasted for many weeks.

These results apparently show that streptococcic infections in the puerperium tend to spontaneous recovery, and that the results are usually good if the patient be not interfered with.

Of course it may be objected that the above results are of no great value, as the infection in most cases was possibly due to streptococci which possessed but a slight degree of virulence. This objection, however, can hardly be maintained when it is considered that the cases in question were spread over a period of three years, and occurred not only in the hospital, but in outdoor and consultation practice as well. And the fact that 10 of the cases impressed Dr. Williams as being seriously ill also speaks against this supposition.

The inherent tendency of streptococcic puerperal infections toward recovery is also demonstrated by the observations of Krönig, who stated that in 56 consecutive cases of streptococcic infection occurring in Leipzig, which were treated in essentially the same manner as Dr. Williams' cases, the mortality was only 4 per cent; and that in the entire number of streptococcus infections which he had observed, 76 in all, the mortality had only been 8 per cent.

The comparatively benign character of streptococcic puerperal infections is also borne out by the experience of Savor, who, as we have already indicated, treated 15 cases of streptococcic infection with antistreptococcic serum, with 1 death. But in spite of these apparently good results, he stated that he believed that the serum had exerted no appreciable influence upon the course of the disease. He designated 8 of his cases as "severe," 6 as "moderate," and 1 as "mild." While treating these 15 cases with antistreptococcic serum, he also observed 24 other cases of streptococcus infection in Chrobak's clinic, which

however, had so improved by the time that he had demonstrated streptococci in his cultures that they did not require further treatment. All of these cases ended in recovery, thus making a series of 39 cases of streptococcic puerperal infection which were treated by Savor, with 1 death, a mortality of 2.59 per cent.

On adding together the cases of Krönig, Savor, and Williams, we obtain a series of 138 cases, in all of which streptococci were demonstrated bacteriologically, with 8 deaths, a mortality of 5.75 per cent.

These observations appear to indicate that the mortality in the average case of streptococcic puerperal infection is not anything like so high as is generally believed, and tend to confirm the supposition of Labadie-Lagrave, who believes that the universal adoption of anti- and aseptic methods in hospital practice has rendered the streptococci, with which one ordinarily has to deal, far less virulent than in the pre-antiseptic days. And one cannot help feeling that the bad results, which are frequently observed in these cases, are due more to the treatment than to the disease itself.

In all probability the series of cases observed by Krönig, Savor, and Williams did not include the same number of severe infections as did the cases which we have collected in our tables, in which streptococci were demonstrated and which were treated by serum. But it would appear to us that the former can be very appropriately compared with the cases which were treated by serum, but in which a bacteriological examination was not made; especially as 104 consecutive cases observed by Wallich were included among them. In this entire series of cases, the great majority of which in all probability were not due to streptococci, the general mortality was 15.85 per cent, whereas the mortality of the 138 cases in question was only 5.75 per cent. And we are inclined to believe that this marked difference was due, in part at least, to the difference in the treatment employed in the two groups of cases.

Dr. Pryor's work was based upon 14 cases, in all of which careful bacteriological examination showed the presence of streptococci. Many of these cases followed abortions, and only a few occurred after full-term deliveries. In all of them the essential method of treatment consisted in a thorough cleansing and attempted sterilization of the uterine cavity, and the packing of the pelvic cavity with iodoform gauze in the

attempt to isolate the uterus from the surrounding structures. Fourteen cases were treated in this way, with only 1 death, a mortality of 7 per cent.

Dr. Fry's work, as may be seen from the appended report, was based upon 8 cases, in all of which streptococci were demonstrated, and all were treated by antistreptococcic serum. After a bacteriological diagnosis was made and the administration of serum commenced, all local treatment was suspended. Three of these cases died, a mortality of 37.5 per cent.

These figures, however, must be taken with a certain amount of reserve, as one of the cases was dying when the serum was first administered, and a second apparently died from causes other than streptococcus infection, thus leaving 6 cases which were treated with serum, with 1 death.

The results obtained by members of your Committee in the treatment of streptococcic puerperal infection are of the greatest possible interest and importance. Williams treated his cases with a single large intrauterine douche of sterile salt solution immediately after taking cultures from the uterine cavity, his further treatment consisting in the administration of large doses of strychnia and alcohol, if indicated by the general condition of the patient. Pryor, on the other hand, opened the posterior cul-de-sac and tightly packed the pelvic cavity with large quantities of iodoform gauze, believing that by this means he could practically isolate the uterus and thereby prevent the extension of the infection to the peritoneum. At the same time he gave large quantities of normal salt solution, either subcutaneously or by the bowel. Fry treated his cases by intrauterine douches until the bacteriological diagnosis of streptococcic infection was made, when all further local treatment was stopped and antistreptococcic serum administered.

Each of these observers has apparently obtained good results by different methods of treatment. Dr. Fry believes that the antistreptococcic serum exerted a markedly beneficial action upon several of his cases. Adding their figures together, we find that Williams has treated 23 cases with 1 death; Pryor, 14 cases with 1 death; and Fry, 6 cases with 1 death (not counting the case which was moribund when first seen), making a total of 43 cases with 3 deaths, or 7 per cent.

When compared with the mortality which is usually ob-



served in puerperal fever, these results appear to be most satisfactory; but, on the other hand, when we recall the statement of Krönig that only 4 per cent of all streptococcic cases die when the patients are practically not treated at all, it would appear that treatment employed by the members of your Committee, whatever it may have been, has not materially influenced the mortality, and the most that we can claim is that we have done our patients no harm by our various methods of treatment.

When we compare our results with those obtained in the total number of cases (352) which were treated by antistreptococcic serum (7 to 20.74 per cent), and to the 101 cases in which streptococci were demonstrated and which were treated with antistreptococcic serum with a mortality of 33 per cent, we are markedly impressed by the high mortality in the cases treated by the serum, and at once attempt to seek an explanation for the marked difference.

On casual consideration it might appear that the high mortality in the latter group of cases was due to the use of the serum. This supposition, however, must be dismissed as untenable, for the reason that no one, excepting Bar and Tissier, and Gaulard, have observed any more serious results from its employment than the occasional production of local abscesses and certain cutaneous eruptions. Savor and Wallich, who have used it in a series of 15 and 104 cases respectively, state that it can be used without appreciable danger to the patient, and these statements are also confirmed by Dr. Fry's experience.

We believe that the very high mortality in the statistics may be explained in part by the fact that many of the observers employed the serum in a few very severe cases only, instead of using it in a large number of consecutive cases of infection. Of course, it is also possible that they may have had to deal with very exceptionally virulent infections, although it is hardly probable that their cases differed materially from our own; especially as Dr. Williams' 23 cases represent the entire number of streptococcus cases which he saw in three years, with the exception of a few consultation cases which were moribund when first seen and from which cultures were not made.

In view of these considerations, it would appear to us that the most rational explanation for the high mortality in the cases reported in the literature is to be found in the fact that the great majority of the cases upon which the statistics are



based were treated by French observers, who curette the puerperal uterus without the slightest hesitation; and on reading their reports it will be found that the great majority of their cases were so treated. The correctness of this supposition is apparently substantiated by the results obtained by Savor, who treated a series of 15 cases with serum, but without curettage, and lost only 1 case. The mortality in his series is much lower than in any other series of streptococcus cases treated with serum with which we are acquainted; and the only explanation which we can offer for it is that he did not use the curette.

When we consider that in the vast majority of streptococcus infections in the puerperium we have to deal simply with an endometritis, in which, according to Bumm and all subsequent observers, the bulk of the streptococci are in the necrotic superficial portions of the endometrium, and are separated from the muscular wall of the uterus and its lymphatics by a protective wall of leucocytes, which is less and less well developed the greater the virulence of the streptococci, it is very easy to understand that curettage, no matter how carefully done, serves to break down this protective wall and to directly infect the deeper layers of the endometrium and the muscularis, from which the infection rapidly spreads to the peritoneum.

We accordingly believe that the curette is a most dangerous instrument in the treatment of streptococcic endometritis; as it is apparently useless in the virulent forms of the infection in which the streptococci are already within the lymphatics and the muscular wall of the uterus, and often converts mild cases into severe ones.

We also believe that the vast majority of cases of streptococcic infection are due to organisms of slight or mild degrees of virulence and tend to recover if let alone; while, when the infection is due to very virulent organisms, the vast majority of patients will die, no matter what our treatment. And we believe that it is better to leave such patients alone, or to treat them by the methods which we have just indicated, rather than to build false hopes upon the efficacy of curettage and the employment of antistreptococcic serum.

It is unnecessary to add that the prognosis in cases with puerperal peritonitis is almost uniformly fatal, and that no method of treatment with which we are familiar will be of any avail.

Your Committee likewise disapproves of the performance of

hysterectomy for puerperal infection in its acute stages; for, if the operation be done sufficiently early to be of value, we feel convinced that many cases will be operated upon unnecessarily; while if the operation be not performed until it is clearly indicated, the results will be almost uniformly fatal. We do not wish to be understood, however, as condemning the operation in certain chronic cases, for then we simply follow the time-honored surgical maxim, "Where there is pus, go after it."

Your Committee would sum up the results of their studies and observations in the following conclusions:

I. A study of the literature shows that 352 cases of puerperal infection have been treated by many observers, with a mortality of 20.74 per cent; where streptococci were positively demonstrated, the mortality was 33 per cent.

II. Marmorek's claim that his antistreptococcic serum will cure streptococcic puerperal infection does not appear to be substantiated by the results thus far reported.

III. Experimental work has cast grave doubts upon the efficiency of antistreptococcic serum in clinical work, by showing that a serum which is obtained from a given streptococcus may protect an animal from that organism, but may be absolutely inefficient against another streptococcus, and that the number of serums which may be prepared is limited only by the number of varieties of streptococci which may exist.

IV. Thus far the only definite result of Marmorek's work is the development of a method by which we can increase the virulence of certain streptococci to an almost inconceivable extent, so that one hundred billionth of a cubic centimetre of a culture will kill a rabbit.

V. The personal experience of your Committee has shown that the mortality of streptococcus endometritis, if not interfered with, is something less than 5 per cent, and that such cases tend to recover if Nature's work is not undone by too energetic local treatment.

VI. We unhesitatingly condemn curettage and total hysterectomy in streptococcus infections after full-term delivery, and attribute a large part of the excessive mortality in the literature to the former operation.

VII. In puerperal infections a portion of the uterine lochia should be removed by Döderlein's tube for bacteriological examination, and an intrauterine douche of four to five litres of sterile salt solution given just afterward. If the infection be due to streptococci, the uterus should not be touched again, and

the patient be given very large doses of strychnia and alcohol if necessary. If the infection be due to other organisms, repeated douchings and even curettage may be advisable.

VIII. If the infection extends toward the peritoneal cavity, and in gravely septicemic cases, Pryor's method of isolating the uterus by packing the pelvis with iodoform gauze may be of service.

IX. The experience of one of the members of the Committee with antistreptococcus serum has shown that it has no deleterious effect upon the patient, and, therefore, may be tried if desired. But we find nothing in the clinical or experimental literature or in our own experience to indicate that its employment will materially improve the general results in the treatment of streptococcus puerperal infection.

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## II.

## UPON THE TREATMENT OF PUERPERAL STREPTOCOCCUS INFECTION BY CURETTAGE, THE CUL DE-SAC INCISION, AND THE APPLICATION OF ANTISEPTIC DRESSINGS.

REPORT OF DR. WILLIAM R. PRYOR.

Although I have employed the method for eight years, I excluded from this report all cases in which bacteriological examination has failed to find streptococci in *both* the contents of the uterus and in the pelvic cavity. My report embraces 14 cases in which such infection has been proven. There were many other vaginal sections which showed other pathogenic germs, and other cases of streptococcus infection which were subjected to vaginal hysterectomy. All of these are excluded.

The gravity of puerperal streptococcus infection is directly in proportion to the amount of tissue involved and the state of the uterus at the time of infection. Thus we see that an organ criminally aborted at the third month, with much trauma inflicted upon it, will produce graver symptoms than accompany a similar infection implanted upon a placental tuft in a full-term uterus which has not been bruised.

I am also convinced that there is a marked difference in the virulence of the germ in different epidemics and in different localities.

Inasmuch as streptococcus puerperal infection is essentially a wound infection, it is doing too little to treat the septicemia and ignore the local lesions. And as trauma tends to spread the infection, as well as render the type more grave, operative procedures which do not accomplish the destruction of the invading germs are to be condemned. Curettage alone is pre-eminently such an operation. The injection of strong antiseptics into the uterus is likewise, and for the same reason, condemned.

The cases reported were subjected to the following treatment:

Where the case warranted delay in operating, I began a careful preparation of the patient, the object of which was to reduce the specific gravity of the urine and lower the per cent of urea and to cleanse the colon. To accomplish this such cases were given high colon enemata of four pints of normal salt solution every eight hours. As a result the temperature and pulse fell.

Case X. Y. Za.	1.5°.	Pulse 20 beats.	
Case X. Y. Z.	1.2°.	" 18	"
Case U. V.	1.2°.	" 12	"
Case Q. R.	2.6°.	" 2	"
Case O. P.	1°.	" 6	" (rose).
Case G. H.	1.4°.	" 16	"
Case A. B.	2.5°.	" 20	"

In the emergency operations the observation of the effect of the saline infusions is masked by the operation; but uniformly in such cases have we observed a decrease in the per cent of urea and in the specific gravity; also, where albumin was present before the operation, we have observed that it either disappeared or was markedly diminished by the infusions of salt solution.

The operation consists in a thorough curettage of the uterus, careful removal of all *débris*, and irrigation with salt solution; and then a broad incision into Douglas' pouch, the liberation of all adherent organs, the evacuation of all fluids, and the application of enough iodoform gauze to completely fill all portions of the pelvis posterior to the uterus, and tight packing of the uterus by the same material. The curettage is performed as much for the purpose of creating a raw surface which can rapidly absorb iodine as to remove infected tissue.

The cul-de-sac incision seeks the evacuation of all fluids, but the chief object sought is the application of iodoform dressings to all parts of the pelvic peritoneum to secure isolation and sterilization of the infected field.

A strong reaction of iodine is gotten from the urine in an average of five hours after the operation. In cases which show pus the absorption of iodine is not so rapid as in the cases of acute pelvic lymphangitis, and the latter are the grave cases which demand speedy iodism. Two hours after operating iodine has been found in the urine. It is necessary to secure rapid elimination of the iodine. This is obtained in grave cases by intravenous infusion of salt solution, and in all cases by high colon injections of salt solution frequently repeated.

We have determined that a rise in specific gravity does not necessarily show a rise in per cent of urea, but rather indicates the amount of iodine eliminated. The presence of nephritis retards the elimination of iodine, and therefore emphasizes the necessity for intravenous infusion in such cases.

We have found that iodine in the urine causes a precipitate with Fehling's solution in testing for sugar, hence Nylander's

test for sugar should be used. In testing fresh urine for iodine we have found the chloroform-nitric-acid test the best and most sensitive qualitative test.

I am unable to precisely state what effect the presence of iodine in the blood has upon the septicemia, but a study of the charts would indicate that more is accomplished by the iodine than a mere sterilization of the pelvis.

In no case, save case I. J., were streptococci found later than the third dressing, and in that case the fifth dressing was free from them. Our observations have shown that all cocci are destroyed by the method of treatment, but that the colon bacillus remains constantly present.

### III.

#### THE ANTISTREPTOCOCCIC SERUM IN THE TREATMENT OF PUERPERAL SEPSIS.

REPORT OF DR. HENRY D. FRY.

Since the last meeting of the Society further observations have been made regarding the value of antistreptococcic serum in the treatment of puerperal sepsis. The cases which have come under my observation were met with chiefly in Columbia Lying-in Hospital, and occurred in my service and in that of Drs. J. W. Bovée and J. F. Moran, to whom I am under obligations for the courtesy of being permitted to use their material, and to the pathologist of the institution, Dr. John Carroll, for his careful postmortem and bacteriological examinations. One case was seen in consultation with Dr. Henry B. Deale, and two occurred in my own clientèle.

In all cases of fever after childbirth, cultures were promptly taken from the uterine cavity with sterilized glass tube and submitted to the bacteriologist. Infection due to the staphylococcus, colon bacillus, saprophytic germs, etc., was eliminated, and the serum treatment employed only in streptococcic infection, pure or mixed.

The local treatment employed in those cases over which I had personal control was a preliminary and thorough cleansing of the utero-vaginal canal with an antiseptic douche. The uterine cavity was let alone as soon as the diagnosis of streptococcic infection was made. The curette was not used unless saprophytic germs were also present. Puerperal ulcers of the cervix, vagina, or outlet were cauterized. Vaginal douches of hot sterilized water or boracic acid solutions were given three times



daily. Besides the injection of antistreptococcic serum the constitutional treatment was limited to stimulating and sustaining remedies. The serum treatment was begun as soon as the diagnosis of streptococcic infection was made. In exceptional cases, when the clinical aspect pointed strongly to streptococcic infection, the treatment was commenced before knowing the result of the cultures.

CASE I. *Abortion; Sepsis; Streptococci in Pure Culture; Serum Injections; Panhysterectomy; Death.*—E. M., American, married, age 25 years, Ipara, entered Columbia Hospital on the evening of July 25, 1898, suffering from uterine pain and hemorrhage. The history could not be ascertained, but suspicions pointed to a criminal attempt to interfere with gestation. The perineum and cervix were lacerated, the uterus was large and soft, the cervix partially dilated, membranes protruding. Iodoform gauze tampon in the vagina controlled bleeding, and about three hours after admission she passed a four-months fetus.

July 26: 9 A.M., pulse 116, temperature 103.8°. Perspired freely during day and evening; temperature fell to 98.2°.

July 27: 9 A.M., pulse 78, temperature 98°. 10 A.M., chill, followed by rise of temperature to 104.8°. Curettage and intra-uterine douche. 4 P.M., pulse 92, temperature 100°. Recurrence of chill, and night temperature 105°.

July 28 and 29: Temperature varied from 100.8° to 105°. Vaginal and intrauterine douches administered. Cultures of intrauterine discharge showed streptococci.

July 30: 10 cubic centimetres of antistreptococcic serum injected at 7:30 P.M. and repeated at midnight.

From this date 10 cubic centimetres of serum were given each day at noon until August 5. The immediate effect of the serum was striking. Before administration the patient was delirious, pulse rapid and feeble, respirations accelerated; there was a cough, and moist râles were diffused over both lungs posteriorly. After 20 cubic centimetres had been injected all symptoms improved and the mind cleared up; pulse dropped to 76, temperature 98.6°. For the succeeding four days the pulse varied from 60 to 74, and the temperature from 98° to 100.2°, except two short rises to 103°. From August 6 the excursions of temperature were greater; recurrent chills were followed by high fever. The serum appeared gradually to lose its effect, and the patient grew worse. On August 17 it was discontinued, the patient having received 100 cubic centi-



metres. Microscopic examination of the blood was negative. August 20 panhysterectomy was performed. The uterus was enlarged and softened. The right Fallopian tube near its uterine end was gangrenous, and in the centre of this tissue was an opening large enough to admit the end of the finger. Tissues friable and hemorrhage difficult to control. Patient died soon after operation.

*Autopsy, about four hours after death.*—The skin of the whole body has a sallow, greenish hue; fairly good layer of subcutaneous fat. Pleural sacs free from fluid; no adhesions between lungs and thoracic wall. Right lung shows a number of small subpleural petechial hemorrhages upon all of the lobes; the left lung, only a few. Numerous small infarctions upon the surfaces of both lungs, several recent hemorrhagic infarctions of good size in the middle lobe of the left lung. A firm, caseous, nodular mass, as large as a small hazelnut, just within the upper lateral margin of the lower lobe, causing inflammatory adhesion to the lobe above, and an interlobar pleurisy with numerous delicate dry adhesions. Small multilocular cavity at the apex, containing a small amount of thin, dirty-looking, blood-stained material. Lung slightly edematous throughout. Pleural surface of the right lung dull from thin layer of fibrinous exudate; lobes united by dry, delicate adhesions similar to those on the left side. Embolic infarcts on the surfaces of both lungs are slightly raised, of an average diameter of about 8 to 10 millimetres, and the tissue is edematous and inflamed and rises above the cut surface. This does not apply to the solid red infarcts in the left lung. Pericardium contains about two ounces of clear, straw-colored serum. Heart considerably enlarged; right cavities dilated, left contracted. No marked hypertrophy or atrophy of ventricular walls. Aortic valves, though competent by the water test, show distinctly raised calcareous plates just above the points of junction of the cusps and between the sinuses of Valsalva. Each plate occupies an area of about 10 millimetres. Abdominal cavity contains about a quart of thin, blood-stained, watery fluid. Omentum injected. Liver pale and enlarged; the right lobe reaches downward to a point on a level with the junction of the third and fourth lumbar vertebræ. Cut surface is of a brown clay color, shows no markings, bleeds only from the larger vessels, is firm and resistant. Intestines pale, their mucous membrane generally normal. A few small hemorrhages of the mucous membrane of the ileum. Interior of stomach normal. Both layers of the pelvic peritoneum

dotted with numerous petechial hemorrhages and large areas of extravasation. About three inches of the jejunum invaginated, but easily released. Left kidney a little enlarged, pale, capsule injected, and shows a few punctiform hemorrhages. Tissue extremely pale. Malpighian bodies can be made out with difficulty; pyramids very pale. Right kidney slightly smaller than the left, same general appearances; pyramids almost indistinguishable from the cortex. In both organs the cortex is of a dull clay color and entirely free from markings. Capsules slightly adherent. Spleen enormously enlarged, smooth, and covered with a light layer of lymph. Upon section it is somewhat muddy-looking and of a dull brick-red color, interstitial elements apparently increased. Consistence moderately firm, though easily broken down.

*Cultures.*—Abdominal cavity: micrococcus in pairs and short chains of four or six; bacillus moderately thick and varying in length, some long threads. Blood: sterile. Bile: small coccus in pairs, some forms lanceolate. Urine: no growth. Liver, kidney, spleen: micrococcus and bacillus same as above. No streptococci were obtained at any time.

CASE II. *Multipara; Abortion; Sepsis; Streptococci in Pure Culture; Hysterectomy; Delayed Use of Serum; Death.*—L. A., white, age 33 years, Vpara, entered Columbia Hospital in the service of Dr. Bovée on August 23, 1898. Last child was born five years ago; has had two miscarriages, the present illness dating from the last miscarriage about three weeks ago. When three or four months pregnant she had attempted to produce a miscarriage by the use of drugs. Failing in this she had consulted a woman, who succeeded by using a sharp instrument.

She suffered from chills, fever, and sweating, and was much worse during the four or five days immediately preceding her admission to the hospital. Pulse on admission 98, temperature 101.8°; tongue badly coated; breath foul; diarrhea. Examination showed the uterus enlarged; cervix softened, gaping, and discharging a profuse, sero-sanguinolent fluid of disagreeable odor. A mass the size of an egg was detected in the right side of the pelvis. Vaginal douches of carbolic acid solution were given every four hours, and the temperature dropped to 99.2° and the pulse to 88.

August 25: 1 P.M., severe chill followed by rise of temperature to 105°.

August 26: Curettage. Secretions from the uterus showed streptococci in pure culture.

August 28: Hysterectomy and double salpingo-oöphorectomy. The pelvis contained eight or ten ounces of serous fluid. Uterus enlarged, tubes swollen and congested. The right tube was more involved, the fimbriæ were congested, and a drop of pus issued from the tubal opening. The tissues being soft and pliable, some difficulty was experienced in controlling bleeding. Gauze drainage was used through the vagina. Patient stood the operation well and remained in fairly good condition during the next twenty-four hours.

August 29: Pulse became rapid in spite of free stimulation. The next day I took charge of the case in Dr. Bovée's absence from the city, and ordered antistreptococcic serum.

August 30: 12 M., 10 cubic centimetres of antistreptococcic serum injected, 5 cubic centimetres given at 9 P.M., and 5 cubic centimetres at 11 P.M.

August 31: 6 A.M., patient died.

*Autopsy, five hours after death.*—Body warm, well nourished; no rigor mortis. Omentum fatty, congested, and adherent to the small intestines, which were deeply injected and showed numerous ecchymoses. Pelvic cavity contained about eight ounces of blood-stained serous fluid. Pleural sacs contained about the normal amount of fluid. Visceral and parietal membranes deeply injected. Lungs congested and edematous. Cut surfaces exude blood and a purulent looking fluid. Heart large, cavities distended, left ventricle hypertrophied, insufficiency of pulmonic and aortic valves. Pericardial sac contains no excess of fluid. Liver enlarged, right lobe reaching down to bifurcation of the aorta. Anterior surface mottled, posterior congested. Peritoneal surface of the gall bladder deeply injected, also the under and posterior surfaces of the liver. Spleen deeply congested, enlarged, soft, pulpy consistence, and breaks down easily. Kidneys enlarged, stellate veins congested, cortex increased in thickness and striated. Well-marked parenchymatous degeneration. Pyramids dark and congested. Pelvic glands enlarged and firm. About the head of the pancreas was a considerable amount of pus.

*Cultures.*—Blood, bile, liver, and kidney: sterile. Spleen: staphylococcus pyogenes aureus.<sup>1</sup> Lungs, and pus in the

<sup>1</sup> "A possible explanation of the failure to obtain the streptococcus from the spleen is that, the culture being taken on agar slants, a few colonies only may have developed and they may have shown only the staphylococcus forms when stained, as occurs frequently when the streptococcus is cultivated upon the surface of solid media."—DR. CARROLL.



abdominal cavity: streptococcus pyogenes and staphylococcus pyogenes aureus.

CASE III. *Primipara; Labor at Term; Fever Fourth Day; Infection due to Streptococcus; Temperature Normal on Eleventh Day; Relapse; Serum Injections renewed with Negative Result; Recovery.*—(Dr. Deale.) Mrs. S. F. H., age 30, white, primipara; delivered on November 4, 1898, after a short and easy labor, of a healthy female child. Only one examination before delivery and none afterward; no douches given.

November 8: Slight chill, with moderate rise of temperature,  $101^{\circ}$ .

November 9: Severe chill; temperature rose to  $104^{\circ}$ . Vaginal douches given.

November 10: Morning temperature,  $104^{\circ}$ . I saw the case in consultation and took a culture of the uterine discharge. Reported later pure streptococcic infection. Intrauterine irrigation of carbolic acid solution. Five cubic centimetres of serum injected. 10:30 P.M.,  $103.6^{\circ}$ , 5 cubic centimetres of serum administered.

November 11: 8 A.M., temperature  $102.4^{\circ}$ ; 3 P.M.,  $103.6^{\circ}$ ; 8 P.M.,  $102.6^{\circ}$ , 10 cubic centimetres of serum. Intrauterine and vaginal douches continued.

November 12: 8 A.M.,  $102.6^{\circ}$ ; 3 P.M.,  $105^{\circ}$ . Ten cubic centimetres of serum injected at 3 P.M., repeated at 8 P.M.

November 13: 8 A.M.,  $102.4^{\circ}$ , 10 cubic centimetres of serum; 8 P.M.,  $102.6^{\circ}$ , 5 cubic centimetres of serum.

November 14: 8 A.M.,  $99.6^{\circ}$ , 10 cubic centimetres of serum; 8 P.M.,  $100.6^{\circ}$ .

November 15: 8 A.M.,  $98.4^{\circ}$ ; 8 P.M.,  $99.8^{\circ}$ .

November 16: 8 A.M.,  $98.5^{\circ}$ ; 8 P.M.,  $99.6^{\circ}$ .

November 17: 8 A.M.,  $98.4^{\circ}$ ; 8 P.M.,  $100.2^{\circ}$ .

November 18: 8 A.M.,  $103.2^{\circ}$ , 10 cubic centimetres of serum injected; 4 P.M.,  $104.6^{\circ}$ .

November 19: 8 A.M.,  $103.6^{\circ}$ , 10 cubic centimetres of serum; 4 P.M.,  $104.2^{\circ}$ , 10 cubic centimetres of serum.

November 20: 8 A.M.,  $103.2^{\circ}$ , 10 cubic centimetres of serum; 8 P.M.,  $102.6^{\circ}$ ; 12 midnight,  $104.2^{\circ}$ .

November 21: 8 A.M.,  $101.8^{\circ}$ ; 8 P.M.,  $102.6^{\circ}$ .

November 22: 8 A.M.,  $102.8^{\circ}$ ; 8 P.M.,  $103^{\circ}$ , 5 cubic centimetres of serum.

November 23: 8 A.M.,  $103.2^{\circ}$ , 10 cubic centimetres of serum; 8 P.M.,  $103.8^{\circ}$ .



November 24: 8 A.M., 103.6°, 10 cubic centimetres of serum; 8 P.M., 104°, 10 cubic centimetres of serum.

November 25: 8 A.M., 104°, 10 cubic centimetres of serum; 4 P.M., 98.5°.

November 26: 8 A.M., 100.8°; 8 P.M., 100°.

November 27: 8 A.M., 97.6°; 8 P.M., 97.6°.

After this date the temperature continued normal or sub-normal with uninterrupted convalescence. Douches, both intrauterine and vaginal, were continued for ten days until the irrigating fluid came away perfectly clear.

During the attack the patient's mother, who had assisted in taking care of her, developed a facial erysipelas which yielded to the injections of antistreptococcic serum.

CASE IV. *Normal Labor; Sepsis; Streptococcic Infection; Serum; Relapse; Recovery.*—(Moran.) Mrs. A., American, age 33 years, IIIpara, was delivered at Columbia Hospital November 18, 1898. Labor normal and placenta delivered spontaneously twenty minutes later. No vaginal examination had been made during or after labor.

November 19: 9 A.M., pulse 72, temperature 98°. 10 A.M., severe chill followed by rise of pulse to 128 and temperature to 104°. Headache, vomiting, and severe pain in lower part of abdomen. Culture taken. 7 P.M., pulse 130, temperature 103.8°. Uterus large; intrauterine douche of sterile water.

November 20: 9 A.M., pulse 104, temperature 102.2°. Chilly sensation and rise of temperature to 104°. Bacteriological examination of culture showed pure streptococcic infection. 2 P.M., 10 cubic centimetres of serum injected and same quantity repeated at 7 P.M. Temperature fell to 98°, pulse 80, at noon next day. Fever increasing later, 10 cubic centimetres of serum given at 4 and 6 P.M. At midnight pulse was 88, temperature 102.2°.

November 22: 6 A.M., pulse 84, temperature 100°. 9 A.M., pulse 90, temperature 101.8°; 10 cubic centimetres of serum injected, repeated at 6 P.M. Gradual decline of temperature during the night. 3 A.M., pulse 72, temperature 97.4°.

November 23: Slight rise, and at 9 A.M. temperature was 101.6°; 10 cubic centimetres of serum given. 2 P.M., pulse 102, temperature 104°. Ten cubic centimetres at 6 and 9 P.M. Temperature dropped to normal, and, with the exception of slight rise due to subcutaneous abscess, there was no further trouble.

CASE V. *Primipara; Labor at Term; Fever beginning on Sixth Day; Streptococcus; Serum; Recovery* (Fry).—R.

McP., American, age 20 years, Ipara, admitted to Columbia Hospital November 14, 1898. Delivered November 23 at 2 P.M.

November 25: Culture taken from vagina and cervix showed streptococcus pyogenes. Pulse and temperature satisfactory until the afternoon of November 28 (sixth day), when they registered at 4 P.M. 94 and  $102.4^{\circ}$  respectively. 8 P.M., serum, 10 cubic centimetres, injected. Temperature ran about  $101^{\circ}$  for next twenty-four hours.

November 29: 3 A.M., pulse 96, temperature  $102.4^{\circ}$ . Intra-uterine douche of two per cent solution of carbolic acid. 12 M., 10 cubic centimetres of serum administered and repeated at 6 P.M. Temperature gradually dropped until at noon November 30 it was  $99.4^{\circ}$ . At 6 P.M. it was  $100.2^{\circ}$ ; 10 cubic centimetres serum given. Temperature continued to fall and reached normal at 6 P.M. December 1, 10 cubic centimetres were given, and patient made good recovery.

The only local treatment besides one intrauterine injection was hot vaginal douches of sterilized water three times daily.

CASE VI. *Normal Labor; Fever; Streptococcus and Staphylococcus; Serum; Prompt Recovery.*—(Moran). J.S., American, married, Ipara, admitted to Columbia Hospital December 19, 1898. Patient was in labor when she came in, and at 6 P.M. was delivered. Her condition was satisfactory until

December 22, 4 P.M., when chilly sensations and headache accompanied by rise of pulse and temperature to 112 and  $103^{\circ}$  respectively. Culture of uterine secretion taken.

December 23: Morning, pulse 110, temperature  $102.4^{\circ}$ . 11 A.M., 10 cubic centimetres of serum injected. 4 P.M., pulse 112, temperature  $103.6^{\circ}$ . 8 P.M., 20 cubic centimetres of antistreptococcic serum injected. Temperature dropped promptly and on December 24, 9 A.M., was  $99.4^{\circ}$ , pulse 88.

Patient made good convalescence. Culture showed streptococcus and staphylococcus.

CASE VII. *Labor Easy; Postpartum Hemorrhage; Sepsis; Streptococcic Infection; Serum; Recovery.*—(Fry.) Mrs. M., white, age 35 years, IIIpara, no miscarriages. Delivered March 15, 1899, at 9:30 P.M. Labor easy and natural; placenta partially adherent and its removal followed by uterine relaxation and hemorrhage. Sterilized gauze inserted *in utero* promptly checked bleeding. Patient passed a comfortable night.

March 16: 7 A.M., pulse 90, temperature  $100.2^{\circ}$ . Citrate of

magnesia, quinine, vaginal douche of carbolic acid solution. 6 P.M., pulse 106, temperature 103.6°. Bowels moved.

March 17: Morning, pulse 90, temperature 101.2°; intrauterine douche of carbolic acid solution. Evening. pulse 106, temperature 103.8°.

March 18: 7 A.M., pulse 98, temperature 101.2°; intrauterine douche. 2 P.M., pulse 100, temperature 103.8°; intrauterine douche.

March 19: 7 A.M., pulse 100, temperature 103.8°. Large solid stool. 12 M., intrauterine douche. Cervix large, soft, and covered with grayish exudate. Culture taken of uterine discharge. 4 P.M., temperature 104.4°; injection of 6 cubic centimetres of antistreptococcic serum. Temperature dropped in a few hours to 101.8°. 9 P.M., temperature had gone up to 103.9°; 6 cubic centimetres of serum injected.

March 20: 7 A.M., pulse 100, temperature 101.8°; serum injection of 10 cubic centimetres. 3 P.M., pulse 100, temperature 103.8°; 8 cubic centimetres injected.

March 21: 7 A.M., pulse 96, temperature 101°. 4 P.M., pulse 106, temperature 103°.

March 22: 7 A.M., temperature 100°. 9 P.M., pulse 78, temperature 99°.

March 23: Temperature normal.

After the first injection of serum local treatment was discontinued, except to use vaginal douches of boracic acid solution. Report of bacteriological examination of the secretion from the uterus showed streptococcus in pure culture.

CASE VIII. *Primipara; Labor at Term; Acute Sepsis; Streptococcic Infection; Serum Injection; Death in Twenty-four Hours.*—(Fry.) M. de S., primipara, age 26 years, native of Switzerland, passed through her gestation satisfactorily. External examination at eighth month revealed normal pelvic measurements; head well engaged in the pelvic cavity in R. O. P. position.

Labor began on the evening of April 10, 1899. Pains during the night of moderate severity. April 11, 8 A.M.: Dilatation about the size of silver half-dollar. Membranes ruptured spontaneously. Pains increased, and at 1 P.M. dilatation nearly completed. Flexion of head imperfect and no disposition to anterior rotation of the occiput. Under chloroform narcosis the head was rotated manually, but soon returned again to occipito-posterior. Manual rotation repeated and forceps applied. At 2 P.M. head delivered readily; no laceration



of perineum. Placenta expelled by Credé method twenty minutes after the birth of the child. Uterus firmly retracted. Patient's pulse 64. April 12: Passed a comfortable night. At 7 A.M. vomiting set in, followed by diarrhea. Marked depression of circulation; pulse rapid and feeble; cyanosis of lips and extremities; conjunctivæ injected. Strychnia hypodermatically and whiskey freely by mouth. Pulse 140, temperature 100.8°. 1 P.M., heart's action depressed in spite of free stimulation; cyanosis marked; dyspnea. Culture from uterine cavity. Intrauterine douche of two per cent solution of carbolic acid. Scarlatinaform rash over chest and back; some pharyngitis. Pulse rapid and feeble; temperature ran about two degrees above normal. Twenty cubic centimetres of anti-streptococcic serum injected. The eruption extended down the back and over the thighs. Patient took and retained whiskey in large quantities. Strychnia kept up by hypodermatic injections. Exhaustion increased, and patient died at 7 A.M. April 13.

The culture showed pure streptococcus.

The labor had been conducted under rigid antiseptic precautions. The patient had had a soap and warm-water bath at the onset of labor. The genitalia had been washed with bichloride solution, and a moist bichloride dressing was kept applied to the vulva throughout the labor. The hands had been prepared at each examination—scrubbed with soap and hot water, immersed in saturated solutions of permanganate of potassium, of oxalic acid, and finally in bichloride solution 1:1000. The forceps had been carefully sterilized. It is open to suspicion whether scarlet-fever poison may not have entered as a factor in the case, as slight evidence existed of exposure to contagion.

*Summary.*—The report of 8 cases of infection from the streptococcus is here recorded. Two occurred after criminal abortion and 6 after labor at full term. Of the 8 cases 3 died and 5 recovered. Two of the fatal cases followed infection from criminal abortion; both had been curetted and afterward subjected to total hysterectomy. The remaining fatal case was one of fulminating sepsis.

Case 1 apparently improved after the injection of 20 cubic centimetres of serum, begun on the fifth day after the disease. During the first seven days 50 cubic centimetres were administered with satisfactory result. No streptococci were found in the cultures made post mortem. The recurrent fever did not

respond to the further use of the serum, probably because it was due secondary infection from the bacillus of putrefaction. This bacillus was found in cultures, made after death, from the abdominal cavity, liver, kidney, and spleen. At the operation the site of infection was shown by the destructive effect upon the tissues, producing gangrene and perforation of the uterine end of the right Fallopian tube. It is evident that the infection with the bacillus occurred after the culture was taken from the uterine cavity on the fourth day and was introduced during the intrauterine irrigation.

In Case 2 the culture showed pure streptococcus. The infection had existed for three weeks before coming under observation. The serum treatment was begun only eighteen hours before death. The staphylococcus pyogenes aureus was not found in the culture taken from the uterus, but was discovered post mortem in the organs and in the pus in the abdominal cavity. It was probably introduced during the surgical operation. Streptococci were found in the lungs and in the pus in the abdominal cavity, demonstrating that the serum had not had sufficient time to destroy them.

Cases 5 and 7 were evidently pure streptococcic infection. In Case 5 the streptococcus was found in cultures from the vagina and uterus on the second day after labor and four days before the development of infection. Serum injections were begun on the first day, and 50 cubic centimetres in all were administered. The temperature declined steadily and reached normal on the fourth day. One intrauterine irrigation was given on the first day, and afterward three vaginal douches daily of hot sterilized water.

In Case 7 the culture was taken on the fourth day and serum injections begun at the same time; 30 cubic centimetres were injected. The temperature dropped to normal in three days. The uterine cavity was irrigated with a two per cent solution of carbolic acid four times, and vaginal douches of boric acid solution were kept up daily during the treatment. The effect of the intrauterine irrigation was negative, and it was discontinued after the fourth day, when the serum treatment was commenced.

Case 6 was practically pure streptococcic infection. The staphylococcus found in culture with it was evidently not pathogenic. The serum treatment was begun the latter part of the first day, and the pulse and temperature fell to normal in forty-eight hours. The total amount of serum injected was 30 cubic centimetres.

Cases 3 and 4 responded at first to serum injections, the temperature falling to normal in twenty-four hours in Case 4, and on the fourth day of treatment in Case 3. Relapse occurred immediately in the former case, and fever lasted three days longer. In the other, recurrence of fever lasting ten days was preceded by a normal temperature for three mornings, with slight evening elevations. The reports of the culture of the uterus were pure streptococcic infection in both cases. A possible explanation is that the serum antagonized the streptococcic infection represented by the primary fever in each case, and that the relapses were due to secondary infections, over which the antistreptococcic serum exerted no controlling influence.

If this conclusion be correct it points to the importance of repeating the cultures made from the uterine cavity in such cases, with a view of determining, first, whether the serum injections have destroyed the streptococci; second, whether the recurrent fever be due to secondary infection, and, if so, to ascertain the nature of the infecting agent. The danger of intrauterine treatment in cases of pure streptococcic infection is also emphasized by these cases. The strictest antiseptic precautions are necessary to avoid the introduction of secondary infection. Curettage is contraindicated in pure streptococcic infection. If any benefit is to be derived from the use of antistreptococcic serum in a given case of infection, it will respond to the injection of 20 to 30 cubic centimetres of serum, and from 30 to 50 cubic centimetres will control responsive cases if treatment be commenced early.



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